PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

Amersham Biosciences AB
Patent Department
Björkgatan 30
751 84 Uppsala
Sverige

26 Jan 06
RP ✓
AK ✓
1/12/05
PU03100-PCT

PCT

WRITTEN OPINION OF THE INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

(PCT Rule 66)

Date of mailing *(day/month/year)*	28-11-2005
Applicant's or agent's file reference: PU03100-PCT	REPLY DUE: within 60 days from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/SE2004/002007 ✓	2004-12-21 ✓	2003-12-23

International Patent Classification (IPC) or both national classification and IPC
See Supplemental Box

Applicant
Amersham Biosciences AB et al

1. ☒ The written opinion established by the International Searching Authority:
   ☒ is ☐ is not
   considered to be a written opinion of the International Preliminary Examining Authority.

2. This second (first, etc.) opinion contains indications relating to the following items:
   - ☒ Box No. I Basis of the opinion
   - ☐ Box No. II Priority
   - ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☒ Box No. VIII Certain observations on the international application

3. The applicant is hereby invited to reply to this opinion.
   When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(e).
   How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.
   Also For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4*bis*. For an informal communication with the examiner, see Rule 66.6. For an additional opportunity to submit amendments, see Rule 66.4.
   If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary report on patentability (Chapter II of the PCT) must be established according to Rule 69.2 is: 2006-04-23

Name and mailing address of the IPEA/SE	Authorized officer
Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. 46 8 667 72 88	Yvonne Siösteen/ELY Telephone No. 46 8 782 25 00

Form PCT/IPEA/408 (cover sheet) (April 2005)

International application No.
PCT/SE2004/002007

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Cover sheet

B01D 15/00 (2006.01)
B01J 20/22 (2006.01)
B01J 20/32 (2006.01)
C07K 1/20 (2006.01)
C07K 16/06 (2006.01).

WRITTEN OPINION OF THE INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

International application No.
PCT/SE2004/002007

Box No. I Basis of the opinion

1. With regard to the language, this opinion has been established on the basis of:

☐ the international application in the language in which it was filed

☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of:

- ☐ international search (Rules 12.3(a) and 23.1(b))
- ☐ publication of the international application (Rule 12.4(a))
- ☐ international preliminary examination (Rules 55.2(a) and/or 55.3(a))

2. With regard to the elements of the international application, this opinion has been established on the basis of *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed."):*

☒ the international application as originally filed/furnished

☐ the description:

pages _____ as originally filed/furnished
pages _____ received by this Authority on _____
pages _____ received by this Authority on _____

☐ the claims:

pages _____ as originally filed/furnished
pages _____ as amended (together with any statement) under Article 19
pages _____ received by this Authority on _____
pages _____ received by this Authority on _____

☐ the drawings:

pages _____ as originally filed/furnished
pages _____ received by this Authority on _____
pages _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing *(specify)*: _____
- ☐ any table(s) related to the sequence listing *(specify)*: _____

4. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing *(specify)*: _____
- ☐ any table(s) related to the sequence listing *(specify)*: _____

WRITTEN OPINION OF THE
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

International application No.
PCT/SE2004/002007

Box No. V **Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	
	Claims	
Inventive step (IS)	Claims	1-28 (no)
	Claims	
Industrial applicability (IA)	Claims	
	Claims	

2. Citations and explanations:

The present application pertains to a separation matrix for isolation of antibodies. The matrix is composed of a porous support to which ligands comprising at least one aliphatic sulphonamide have been immobilised. The application also describes a chromatography column which contains the described matrix.

The problem to be solved by the present application is to separate antibodies at a low ion ionic strength and at pH values around neutral. The solution to this problem is to provide a separation matrix according to the claimed invention wherein ligands comprising one or more sulphonamides have been immobilised to a porous support. It is characterized by the R-group of the sulphonyl being an aliphatic compound. A method using the claimed matrix does not require any addition of detergent to achieve adsorption and it enables highly selective adsorption of antibodies.

The following documents, cited in the international search report, are considered to be of particular relevance:

D1: US 4725355
D2: EP 0197521

D1 discloses a body fluid purification medium comprising a support and an adsorbent for separation of pathogenic substances such as immunoglobulins and immune complexes (see column 3, lines 12-26). The matrix comprises a sulphonamide characterised by an R group being hydrogen, methylcarbonyl, guanidine, pyridine, 1,3-diazine, merazine, methazine, isomidine, azole or a derivative thereof (see column 4, lines

.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Box V

1-13). The R group is preferably an aromatic group. The support is capable of selectively adsorbing pathogenic substances in blood.

D2 discloses an immunoglobulin adsorbent which comprises a hydroxyl-containing water-insoluble carrier to which a diamine compound has been attached. The compound has been attached through a silane coupling agent and the R group constitutes of an aromatic group.

D1 is considered to represent the closest prior art.

The claimed matrix differs from the known matrix of D1 in that the R group of the sulphonyl is an aliphatic compound instead of hydrogen, methylcarbonyl, guanidine, pyridine, 1,3-diazine, merazine, methazine, isomidine, azole or a derivative thereof.

The problem to be solved by this difference is to obtain a separation process for immunoglobulins which can be performed at low ionic strength and at pH values around neutral.

However, since it is previously known from D1 a matrix comprising a sulphonyl group wherein the R group can be i.a. hydrogen it is considered to be an obvious alternative for a person skilled in the art to exchange the R group to an aliphatic compound.

Also, the separation matrix can only be considered as patentable if it presents an unexpected effect compared to the known matrixes in the above cited documents. This unexpected effect must also be valid for the whole scope of the claims (see Box VIII).

Claims 1-28 are novel but are not considered to involve an inventive step. The claims are industrially applicable.

WRITTEN OPINION OF THE
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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The claims do not disclose the invention in a sufficiently clear manner. The breath of the claims should be such that it represents a reasonable generalisation of the examples provided, and such that it is credible that every compound falling within the scope actually provides a solution to the problem underlying the invention. See Article 6. The examples in the description relate to sulphonamides wherein the ligand is choosen from cysteamine, triethylenetetramine, diethylenetriamine,pentaethylenehexamine and polyethyleneimine whereas the claims relate to the broad definition "sulphonamides wherein the R group of the sulphonyl is an aliphatic compound".